

CLAIMS

1. A polynucleotide encoding a modified sodium iodide symporter (NIS) protein, the protein having a net electrostatic charge more positive than the net electrostatic charge of a corresponding wild-type NIS protein, wherein expression of the modified NIS protein in a cell results in higher intracellular levels of an NIS substrate than does expression of the same amount of a wild-type NIS protein.

2. The polynucleotide of claim 1, wherein the modified NIS protein comprises from 1 to 19 positively charged amino acids added to the amino acid sequence of a wild-type NIS protein.

3. The polynucleotide of claim 1, wherein the modified NIS protein comprises from 4 to 16 positively charged amino acids added to the amino acid sequence of a wild-type NIS protein.

4. The polynucleotide of claim 1, wherein the modified NIS protein comprises from 6 to 14 positively charged amino acids added to the amino acid sequence of a wild-type NIS protein.

5. The polynucleotide of claim 2, wherein the amino acids added to the amino acid sequence of a wild-type NIS protein comprise at least one continuous sequence of amino acids.

6. The polynucleotide of claim 5, wherein the continuous sequence of amino acids contains only positively charged amino acids.

7. The polynucleotide of claim 2 wherein the amino acids added to the amino acid sequence of a wild-type NIS protein comprise 1, 2 or 3 sequences of continuous amino acids.

8. The polynucleotide of claim 5, wherein the continuous sequence of amino acids comprises at least 1 lysine amino acid.

9. The polynucleotide of claim 5, wherein the continuous sequence of amino acids comprises at least 5 lysine amino acids.

10. The polynucleotide of claim 5, wherein the continuous sequence of amino acids comprises at least 10 lysine amino acids.

11. The polynucleotide of claim 5, wherein the continuous sequence of amino acids is added to the amino terminal end, the carboxyl terminal end, or both the amino terminal and carboxyl terminal ends of a wild-type NIS protein.

12. The polynucleotide of claim 5, wherein the continuous sequence of amino acids is added internal to the carboxyl and amino terminal ends of the wild-type NIS protein.

13. The polynucleotide of claim 12, wherein the continuous sequence of amino acids is added to an extra-membrane domain of the protein.

14. The polynucleotide of claim 13, wherein the extra-membrane domain is an intracellular extra-membrane domain.

15. The polynucleotide of claim 1, wherein the modified NIS protein comprises at least one positively charged amino acid that has replaced at least one uncharged or negatively charged amino acid within the amino acid sequence of a wild-type NIS protein.

16. The polynucleotide of claim 1, wherein the modified NIS protein comprises from 1 to 19 positively charged amino acids that have replaced uncharged or negatively charged amino acids within the amino acid sequence of a wild-type NIS protein.

17. The polynucleotide of claim 1, wherein the modified NIS protein comprises from 4 to 16 positively charged amino acids that have replaced uncharged or negatively charged amino acids within the amino acid sequence of a wild-type NIS protein.

18. The polynucleotide of claim 1, wherein the modified NIS protein comprises from 6 to 14 positively charged amino acids that have replaced uncharged or negatively charged amino acids within the amino acid sequence of a wild-type NIS protein.

19. The polynucleotide of claim 15, wherein the uncharged or negatively charged amino acid is within an intracellular extra-membrane domain of the wild-type NIS protein.

20. The polynucleotide of claim 19, wherein the extra-membrane domain is an intracellular extra-membrane domain.

5 21. The polynucleotide of claim 1, wherein the modified NIS protein comprises at least one uncharged amino acid that has replaced at least one negatively charged amino acid within the amino acid sequence of a wild-type NIS protein.

10 22. The polynucleotide of claim 1, wherein the modified NIS protein comprises one or more additions of positively charged amino acids to the wild-type NIS protein sequence, replacement of one or more amino acids of the wild-type NIS protein sequence, or combinations of additions and replacements.

15 23. An expression vector comprising the polynucleotide sequence of claim 1.

24. A modified sodium iodide symporter (NIS) protein having a net electrostatic charge more positive than the net electrostatic charge of a wild-type NIS protein, wherein expression of the modified NIS protein in a cell results in higher intracellular levels of an NIS substrate than does expression of the same amount of a wild-type NIS protein.

20 25. A method for increasing the intracellular concentration of one or more NIS substrates in a cell, comprising:

- 25 a) introducing a modified NIS protein into the cell; and
b) contacting the cell with one or more NIS substrates;
wherein the NIS substrates are transported into the cell.

26. The method of claim 25, wherein the modified NIS protein is introduced into the cell by an expression vector comprising a polynucleotide encoding a modified NIS protein, and wherein the vector expresses the modified NIS protein in the cell.

30 27. A method for imaging cells or tissues in an individual, comprising the steps of:
a) introducing a modified NIS protein into cells in the individual;
b) administering an NIS substrate to the individual such that the NIS substrate contacts and is transported into cells containing the modified NIS protein; and

- c) imaging the cells that have transported the NIS substrate.

28. The method of claim 27, wherein the modified NIS protein is introduced into the cells by an expression vector comprising a polynucleotide encoding a modified NIS protein, and
5 wherein the vector expresses the modified NIS protein in the cell.

29. A method for treating cancer in an individual, comprising the steps of:
a) introducing a modified NIS protein into cancer cells in the individual; and
b) administering an NIS substrate to the individual such that the NIS
10 substrate contacts and is transported into cancer cells containing the modified NIS protein;
wherein the cancer cells that have transported the NIS substrate have decreased viability or decreased growth rate as compared to cancer cells that have not transported the NIS substrate.

15 30. The method of claim 29, wherein the NIS substrate contains a radioactive isotope.

31. The method of claim 29, wherein the NIS substrate has cytotoxic activity.

32. The method of claim 29, wherein the modified NIS protein is introduced into the
20 cancer cells by an expression vector comprising a polynucleotide encoding a modified NIS protein, and wherein the vector expresses the modified NIS protein in the cell.

33. A method for identifying cells in an individual that express a therapeutic protein encoded by an exogenous polynucleotide, comprising:

25 a) introducing an expression vector comprising a polynucleotide encoding a modified NIS protein and a polynucleotide encoding a therapeutic protein into cells in the individual;

b) expressing the therapeutic protein and the modified NIS protein in the cells into which the vector has been introduced;

30 c) administering an NIS substrate to the individual such that the NIS substrate contacts and is transported into the cells which express the therapeutic protein and the modified NIS protein; and

d) imaging the cells to determine which cells have transported the NIS substrate;

wherein the cells that have transported the NIS substrate are also cells that contain the therapeutic protein encoded by the exogenous polynucleotide.